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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,021	12/02/2003	Timothy W. Lovenberg	JJPR-0043	5495
23377	7590	06/27/2005	EXAMINER	
WOODCOCK WASHBURN LLP ONE LIBERTY PLACE, 46TH FLOOR 1650 MARKET STREET PHILADELPHIA, PA 19103			HAMUD, FOZIA M	
		ART UNIT	PAPER NUMBER	
			1647	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/727,021	LOVENBERG ET AL.
	Examiner	Art Unit
	Fozia M. Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 April 2005.
 2a) This action is FINAL. 2b) This action is non-final.
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 24-40 is/are pending in the application.
 4a) Of the above claim(s) 37 and 39 is/are withdrawn from consideration.
 5) Claim(s) _____ is/are allowed.
 6) Claim(s) 24-36,38 and 40 is/are rejected.
 7) Claim(s) _____ is/are objected to.
 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
 10) The drawing(s) filed on 02 December 2003 is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>03/15/04; 03/04/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions:

1. Applicants' election of the invention of Group I (claims 24-36, 38 and 40) filed on 11 April 2005 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicants' request the they reserve the right to pursue the subject matter of all non-elected claims in one or more related applications, is acknowledged. The restriction requirement is still deemed proper and is therefore made FINAL. Claims 24-36, 38 and 40 are under consideration.

Claims 37 and 39 are withdrawn from consideration by the Examiner as they are drawn to non-elected inventions.

Specification:

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. \

Claim rejections-35 USC § 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 24, 26, 27, 29, 30-36, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

Art Unit: 1647

inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only discloses DNA encoding the human histamine H3 receptor comprising the amino acid sequence set forth in SEQ ID NO:7, and DNA molecule comprising the nucleotide sequence set forth I SEQ ID NO:5, 6 or 8. Therefore, the instant specification provides written description for a method of isolating DNA encoding a homologue of human histamine H3 receptor by using the nucleic acid of SEQ ID NO:5 or 6. The instant specification fails to describe "all possible" DNA molecules that encode all possible" human H3 receptors. As such one of ordinary skill in

the art would not be able to practice the method recited in claims 24, 26, 27, 29, 30-36,

Regarding claim 26, Applicants have not described a fragment of SEQ ID NO: 7, which retains the desired activity.
Claim 26 reads on a fragment of SEQ ID NO: 7 as similarly a dipeptide.

The instant specification does not provide written description for claims drawn to a method of using "all possible" DNA that encode "all possible" human histamine H3 receptors, or a method of producing "all possible" human histamine H3 receptor homologues, or a fragment thereof, because the specification does not disclose the structure of all the nucleic acids that encode "all possible" human H3 receptors.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 115).

The instant specification does not define the infinite number of nucleic acids which are to be used in the claimed method. With the exception of the nucleic acid of SEQ ID NO:5 or 6, which encode the polypeptide of SEQ ID NO: NO:7, the skilled artisan cannot envision the detailed structure of the encompassed nucleic acids to be used in the claimed method, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Lts., 18 USPQ2d 1016. Regarding claims 26 and 29, the instant specification does not disclose the structure of "all possible" nucleic acids that encode the polypeptide of SEQ ID NO:7.

Furthermore, In The Reagents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise

definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Therefore only a method of isolating or producing DNA encoding a human H3 receptor homologue by mixing the nucleic acid of SEQ ID NO:5 or 6, with a sample under highly stringent conditions, allowing the two DNA molecules to hybridize, isolating the hybridized DNA and purifying DNA encoding the homologue and expressing the encoded polypeptide, meets the written description provision of 35 U.S.C. 112, first paragraph. As a result, it does not appear that the inventors were in possession of "all possible" nucleic acid molecules which encode human histamine H3 receptor to be used in the claimed method.

3b. Claims 24, 26, 27, 29-30-36, 38 and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of isolating a DNA encoding a homologue of human H3 receptor or producing said receptor, by contacting a sample DNA with the nucleic acid of SEQ ID NO:5 or 6, allowing the two DNA molecules to hybridize under stringent conditions, and isolating the encoded polypeptide, does not reasonably provide enablement for a method of using "all possible" DNA molecules that encode all possible" human H3 receptors, in a hybridization method and isolating the encoded polypeptide.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant claims 24, 27, 30 and 38 are drawn to a method of using a genus of nucleic acids that are defined, by function alone. Due to the large quantity of experimentation necessary to determine all possible nucleic acids that would hybridize to nucleic acid that encode "all possible" H3 human histamine receptors, and to screen for the ones that encode "all possible" homologues of human H3 receptor, or encode homologues of the polypeptide of SEQ ID NO:7, with at least one amino acid variation,
or a fragment of SEQ ID NO:7, the lack of direction/guidance presented in the specification regarding variants of the nucleic acid that encode homologues of human H3 receptors, the complex nature of the invention, the absence of working examples directed to variants of the nucleic acid, the state of the prior art establishing that structure cannot be predicted due to biological activity, the unpredictability of the effects of mutation on the structure and function of the desired polypeptide, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires substantial guidance with respect to which amino acids in the protein's sequence, if any, would tolerate to modification, and detailed knowledge of the ways in which protein's structure relates to its function. In addition, making "conservative" substitutions does not usually produce predictable results. See, for example Lazar et al (Mol. Cell. Biol., Vol. 8, pp. 1247-1252, 1988(U)) who teach that the conservative substitution of glutamic acid for aspartic acid at position 47 reduced biological function

of transforming growth factor alpha, while "non-conservative" substitutions with alanine or asparagine had no effect (see at least the Abstract). In the absence of such guidance, one skilled in the art would have to proceed with undue trial and error experimentation to screen through a vast number of polypeptides with multiple amino acid modifications to identify those having the functional activity of SEQ ID NO: 7.

Claim rejections-35 USC § 112, second paragraph:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 24-36, 38 and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 24, 27 and 38, recite "...allowing human histamine H3 DNA to hybridize with said DNA....", however, the claims are vague and indefinite, because they fail to recite the specific hybridizations conditions. Furthermore, some DNAs, which hybridize under mild hybridization conditions, may not hybridize under stringent conditions. This rejection could be obviated by supplying specific hybridization conditions, supported by the specification.

4b. Claim 30 recites "...which does not substantially alter biological activity...", however, it is unclear which biological activity is being referred to, and how is said activity altered, is it stimulated or inhibited? Furthermore, "substantially" is a relative term, which is not described in the specification, therefore, it is unclear the extent to

which the desired biological activity be altered, less than 5% or more or less? The metes and bounds of the claim cannot be ascertained.

Claims 25, 26, 28, 29, 31-36 and 40 are rejected under 35 U.S.C. 112, second paragraph, as far as they depend from claims 24, 27 and 38, for the limitations set forth directly above.

Claim rejections-35 USC § 102(e):

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

5a. Claims 24, 27 are rejected under 35 U.S.C § 102(e) as being anticipated by U.S Patent No: 5,882,893 (Goodearl et al. published 16 March 1999; effective filing date 04 December 1997).

Goodearl et al disclose an isolated nucleic acid that shares 97.6% identity to the nucleic acid of DEQ ID NO:5 disclosed in the instant application. The nucleic acid disclosed by Goodearl et al encodes a polypeptide that shares 99.8% identity the

polypeptide of SEQ ID NO:7 disclosed in the current application. Goodearl et al also disclose a method of detecting the presence of allelic variants of the polypeptide they disclosed, by contacting a biological sample that is able to hybridize to their nucleic acid under specific hybridization conditions, such that the allelic variant is detected, (see columns 7 and 8, also see column 56 for the specific hybridization conditions used) (also see attached sequence comparison "A". comparing the nucleic acid of the reference to instant SEQ ID NO:5) .

Claims 24 and 27 are drawn to method of isolating DNA encoding a homologue of human H3 receptor and a method of producing a human homologue H3 receptor by hybridizing the nucleic acid encoding the human H3 receptor to a sample in appropriate conditions and isolating or producing said homologue receptor.

Thus, the method disclosed in the Goederal et al reference would detect a nucleic acid which encodes a polypeptide that shares a high degree of similarity to the polypeptide of SEQ ID NO:7, disclosed in the current application, because the nucleic acid disclosed in the Goodearl et al reference shares 97.6% to the nucleic acid of SEQ ID NO:5 of the instant specification and encodes a polypeptide that shares 99.8% identity the polypeptide of SEQ ID NO:7 disclosed in the current application. Therefore, a complement of a nucleic acid that hybridizes to the nucleic acid disclosed by Goodearl et al, would be expected to encode a polypeptide that is a homologue of the polypeptide of SEQ ID NO:7.

Therefore the Goodearl et al reference anticipates the instant claims 24 and 27 in the absence of any evidence to the contrary.

Conclusion:

6. No claim is allowed.

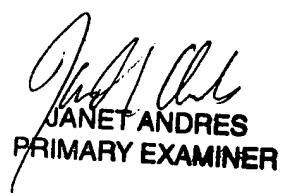
Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
15 June 2005



JANET ANDRES
PRIMARY EXAMINER

Sequence comparison

Patent No. 5886893
GENERAL INFORMATION:
APPLICANT: Andrew D.J. Goodearl
TITLE OF INVENTION: MUSCARINIC RECEPTORS AND USES THEREFOR
NUMBER OF SEQUENCES: 28

Sequence counts in H